Remarks

Claims 18-21, 23, 25, and 27-35 are pending in the subject application and are before the Examiner for consideration.

The present invention provides compounds and ligand libraries comprising two or more triazine groups with attached amine groups (Y) that provide diversity and improved selectivity with respect to protein binding. The compounds of the prior art are not affinity ligands (i.e. small ligand molecules that bind within a larger 3-dimensional binding site of the analyte). Rather, compounds of the prior art form large 3-dimensional pockets that capture small molecules. Thus, they are not affinity ligands.

Claims 18-21, 23, 25 and 27-35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lowik *et al.* (WO 01/42228). The applicants respectfully traverse this ground for rejection because the cited reference does not disclose or suggest the compounds of the claimed invention or their use.

Scheme I of the Lowik *et al.* reference illustrates a method for the synthesis of a macrocycle. The intention of Lowik *et al.* is to form large 3-dimensional pockets that can form binding sites for the capture of small molecules, i.e. the exact opposite of the small affinity ligands of the subject invention.

The Office Action focuses on a single structural difference from the prior art. In doing so, the crux of the current invention is obscured. A key aspect of the compounds of the current invention is that they provide a variety of groups Y. A fundamental purpose of the present invention, and a key distinction from the prior art, is providing multi-dimensional affinity ligand libraries. In a library, the variety of groups Y is important. Their specific structure are not.

The Office Action states that the Lowik *et al.* reference teaches small molecules as ligands. This is not correct. Lowik *et al.* disclose some small molecules, but not as ligands. The Examiner refers to Lowik's Schemes 1 and 6; while non-macrocycles are disclosed, they are not disclosed as ligands. There is certainly no suggestion of ligand libraries.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

The functions and structure of the compounds of Lowik *et al.* and those of the present invention are quite different. The Lowik *et al.* compounds work by capturing the material of interest within the macrocyclic structure; the novel compounds of the current invention work by providing affinity ligands. Therefore, there would be no reason for the skilled artisan to modify the Lowik *et al.* compounds to arrive at the compounds of the current invention.

Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Lowik *et al.* reference.

Claims 18-21, 23, 25 and 27-35 have also been rejected under 35 U.S.C. §103(a) as being unpatentable over Lowik *et al.* (WO 01/42228) and Atkinson *et al.* (GB 2 053,926). The applicants respectfully traverse this ground for rejection because the cited references, taken either alone or in combination, do not disclose or suggest the claimed subject matter.

The Office Action states that Atkinson *et al.* disclose "various triazine compounds useful as affinity chromatography materials," but these do not include a sequence of triazine rings with attached amine Y groups that act as affinity ligands. Combining the references does not give this essential structural feature, i.e. that of affinity ligands, or its effect.

Thus, Atkinson *et al.* does not cure the aforementioned defects of the Lowik *et al.* reference. In particular, there is no suggestion of linking two or more triazine molecules together. By contrast, the presence of the triazine molecules in a specific dimensionality is key to the compounds of the present invention to act as an affinity ligand. It is the diversity created by the triazine framework that provides specific selectivity for certain molecules, and the ease with which that framework can be modified that allows its use for a large number of compounds with respect to protein binding. The molecules disclosed in Atkinson *et al.* are far removed from the present invention.

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969).

There is nothing in the cited references, either taken alone or in combination, to suggest that macrocyclic ring precursors could be used as affinity ligands in their own right, as the intention was to form larger 3-dimensional pockets that would form affinity binding sites for the capture of small molecules.

Thus, one finds neither the suggestion nor the expectation of success in the cited references, either separately or combined. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103.

In view of the foregoing remarks, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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